NeuroNEXT Small Business Innovation in Clinical Trials Direct to Phase II (U44)

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The official link for this solicitation is: http://grants.nih.gov/grants/guide/pa-files/PAR-15-194.html

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Department of Health and Human Services

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PAR-15-194

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001

Description:

Purpose

To facilitate the cooperation and partnering of public and private funding organizations, universities, academic medical centers, research institutes, contract research organizations, biotechnology companies, and pharmaceutical companies, NINDS has formed the Neurology Network of Excellence in Clinical Trials (NeuroNEXT, www.NeuroNEXT.org). NeuroNEXT has a Clinical Coordinating Center (CCC), a Data Coordinating Center (DCC) and a group of 25 geographically distributed clinical sites.

This FOA uses the U44 cooperative agreement mechanism and is open to eligible

applicants, as defined in Section III. Academic researchers may wish to consider applying through PAR-13-343 "NeuroNEXT Clinical Trials (U01)". For-profit organizations and Non-profits other than Institutions of Higher Education may wish to consider applying through PAR-11-344 "NeuroNEXT Infrastructure Resource Access (X01)" if they wish to gain access to the network infrastructure but do not require funds for trial costs.

Definitions

For this funding opportunity announcement, Phase I and II clinical studies or trials refer to the common phases of a clinical trial. SBIR Phase I and II refer to the project phases of the SBIR program.

Scope of the Program

This FOA encourages Direct-to-Phase II SBIR applications for exploratory clinical trials of investigational agents (drugs, biologics, surgical therapies or devices) that may contribute to the justification for and provide the data required for designing a future trial, for biomarker validation studies, or for proof of mechanism clinical studies. Applications for drugs or biologics should provide compelling scientific evidence that the investigational agent proposed for study will reach/act upon the designated target or that its mechanism of action is such that it is expected to be of benefit in ameliorating a specific aspect of the disease. Neurologic diseases chosen for study must fall within the primary responsibility of NINDS (www.ninds.nih.gov/funding/areas/index.htm). Multi-site studies in stroke prevention, treatment and/or recovery are not appropriate for this FOA; those studies would be considered by NIH StrokeNET: http://www.nihstrokenet.org/

Applications in rare diseases are encouraged while recognizing that available patient pools may not be adequate to meet the sample size requirements normally required to establish the efficacy of an intervention. NINDS acknowledges that innovative, non-traditional trial designs including adaptive designs may be appropriate in rare disease studies. While NeuroNEXT is primarily intended for exploratory trials, the network will consider Phase2/3 trials in diseases with a US prevalence of under 5,000 persons.

For this FOA, the small business should have demonstrated the scientific and technical merit and feasibility of the prototype stage of developing a biomedical technology that has commercial potential. The goal of this FOA is to enable a small business that has accomplished the objectives of a Phase I-like SBIR grant through non-SBIR/STTR funds to initiate the Phase II SBIR stage of development, without needing to perform more early stage, Phase-I-SBIR-type research. This FOA will

also not accept ‘regular’ Phase II submissions from SBCs that have received a Phase I SBIR or STTR award from NIH or any other agency that participates in the SBIR/STTR programs. For this FOA, it is expected that the technology, prototype, or method will have passed the proof of principle stage and that the product has demonstrated feasibility and supports a Phase II effort.

Examples of appropriate studies under this FOA include, but are not limited to, those designed to:

- Evaluate and optimize the dose, formulation, safety, tolerability or pharmacokinetics of an intervention in the target population.
- Evaluate whether an intervention produces sufficient evidence of short-term activity (e.g., biomarker activity, pharmacodynamic response, target engagement, dose-response trends) in a human “proof of concept” trial.
- Select or rank the best of two or more potential interventions or dosing regimens to be evaluated in a subsequent trial, based on tolerability, safety data, biological activity, or preliminary clinical efficacy (e.g., futility trials).
- Evaluate biological activity relative to clinical endpoints.

Applications seeking to obtain data needed for pharmacometric modeling are encouraged, with the ultimate aim of enabling the optimal design of a future efficacy trial of an intervention.

For medical devices, in addition to providing initial clinical safety data, appropriate studies are those that inform the next phase of development, usually by finalizing the device design, establishing operator technique, and/or finalizing the choice of study endpoints for the design of a pivotal clinical trial.

This FOA is not intended to support the conduct of a clinical trial where the primary aim is to confirm efficacy of a drug or biologic.

Implementation

Applicants should make note of the following:

(1) Applicants to this FOA will be required to incorporate the NeuroNEXT infrastructure (www.neuronext.org) into their proposed study. Additional (ad-hoc) sites may be proposed to fulfill specific study requirements. All applicants will be required to use the master clinical trial agreements and central IRB that have been established for NeuroNEXT.

(2) Rationale: Exploratory trials primarily test hypotheses in relatively small programs so that the acceptable risk and uncertainty are higher than in later stage programs. Exploratory clinical trials to address an unmet medical need or to improve current

standards of care must anchor their rationale in

- a plausible biological mechanism;
- non-clinical (in vitro and/or in vivo) data; and/or
- early clinical data.

The individual weight should be carefully assessed in the specific context of the application at hand; there is no requirement to provide support from all three areas. If the animal model and efficacy read-out are not sufficiently associated with the human condition, and/or if pre-clinical data (such as for example animal studies) do not sufficiently meet the rigor guidelines, then applicants should consider not using them as primary support of the study rationale.

(3) Secondary Aims:

For drugs and biologics, issues of study feasibility and refinement of study procedures may be addressed as secondary aims in an exploratory clinical trial, but not as the primary aim. Examples of such secondary aims include, but are not limited to, the following:

- Determining the optimal measure (endpoint), its variability, and/or the optimal timing of outcome evaluations in the context of the intervention
- Collecting information on the utility of questionnaires, rating scales, or biomarkers
- For Early Feasibility or Traditional Feasibility studies of medical devices, issues of study feasibility and refinement of study procedures are expected to be addressed as primary aims in addition to providing initial clinical safety data at this stage. These may include:
- Identifying appropriate modifications to the procedure or device to enable a subsequent Pivotal study on a finalized system;
- Refining the intended use population;
- Developing and refining data collection procedures;
- Refining the non-clinical test plans or methodologies; and
- Developing subsequent clinical study protocols.

(4) The NIH recognizes that devices can vary greatly in terms of basic form and function, physiological bases for therapy, degree of invasiveness, etc. Consequently, the appropriate pathway to market may require a traditional Feasibility and Pivotal study in support of an eventual Pre-Market Approval submission, or may require a

more limited study to address specific issues in support of an FDA 510(k) or 510(k) De Novo submission. Clinical studies involving devices may utilize the entire NeuroNEXT Network, or a more limited subset of centers selected based on appropriate expertise for the given device. Investigators are encouraged to contact NINDS Scientific/Research Staff as early as possible to discuss how the NeuroNEXT network may best be utilized in support of their specific device project. NINDS anticipates that the majority of device projects utilizing NeuroNEXT will be traditional Feasibility Studies in order to best leverage the advantages of the network. A Traditional Feasibility Study is a clinical investigation that is commonly used to capture preliminary safety and effectiveness information on a near-final or final device design to adequately plan a Pivotal Study. If an Early Feasibility Study is proposed, it should be designed in accordance with FDA's draft guidance, "Investigational Device Exemptions (IDE) for Early Feasibility Medical Device Clinical Studies, Including Certain First in Human (FIH) Studies", to allow for early clinical evaluation of devices to provide proof of principle and initial clinical safety data while device design and operations are still in development. Early Feasibility and Traditional Feasibility study designs may include single-arm case series, on-off interventions (patients as own controls), device-device comparisons, comparisons to historic controls, comparisons to performance controls, or adaptive/Bayesian designs.

(5) NIH Resources: As appropriate, applicants are encouraged to make use of the following resources for clinical research including:

(a) Clinical and Translational Science Award (CTSA) program (https://www.ctsacentral.org);

(b) NeuroQOL (http://www.neuroqol.org);

(c) NIH Toolbox (http://www.nihtoolbox.org);

(d) PROMIS (http://www.nihpromis.org); and

(e) NINDS Common Data Elements (http://www.commondataelements.ninds.nih.gov).

(6) Mobile Technologies: Applicants are encouraged to consider utilizing (at least experimentally) mobile technologies to facilitate data collection and protocol adherence on the part of research participants and study site staff.

Working with NeuroNEXT is a cooperative venture between the applicant, NINDS, and the NeuroNEXT network. NINDS will provide guidance to potential applicants

with input from NINDS Program Staff and the NeuroNEXT Executive Committee. Potential applicants are strongly encouraged to contact NINDS Scientific/Research Contacts (see Agency Contacts, Section VII) in order to discuss the feasibility of conducting the proposed trial through the NeuroNEXT infrastructure before submitting an application. Pre-application consultation may include an introductory teleconference (at least 3 months prior to submission), followed by a conference call or in-person meeting with NINDS staff, if needed.

The operational clinical protocol and actual budget for trials under this FOA will be constructed after peer review and then reviewed by NINDS for funding consideration. Funding decisions will also be based on a study's fit for the network relative to other proposed and ongoing trials. The award and continuation of funding are subject to milestones to be specified in the notice of grant award according to NINDS policies.
- See more at: http://grants.nih.gov/grants/guide/pa-files/PAR-15-194.html#sthash.K9ci2Zze.dpuf